REMARKS

Claims 1, 3, 6, 8-11, 17, 50, and 52-66 were pending and under consideration. In the present paper, claims 1, 50, 52, and 53 are amended and new claim 67 is presented for consideration. Thus, following entry of the present amendment, claims 1, 3, 6, 8-11, 17, 50, and 52-67 will be pending and under consideration.

Applicants acknowledge the PTO's indication of allowable subject matter in claims 52 and 53 and kindly thank the PTO for the same.

In addition, Applicants kindly thank the Examiner for the courtesy extended in an interview August 2, 2007, with Applicants' representatives Frances Putkey, Nikolaos C. George, and David C. Pauling. In the interview, each of the outstanding objections and rejections was discussed and Applicants' arguments as discussed below were presented to the Examiner. No agreement was reached regarding the patentability of the claims.

I. The Amendments to the Claims

The present paper presents an amendment to claims 1, 50, 52, and 53. The amendments to the claims are fully supported by the application as filed and therefore present no new matter. In particular, the amendment to claim 1 is supported throughout the application as filed and specifically, for example, by the specification at page 11, lines 9-15, at page p, line 6 to page 10, line 17, at page 16, line 19 to page 17, line 10, and at pages 121-122, Table 4. The amendments to claims 50, 52, and 53 merely cancel non-elected subject matter and place claim 50 in independent form by incorporating the limitations of claim 1 and therefore find support, for example, in the originally filed versions of these claims and the portions of the application cited as exemplary support for the amendment to claim 1. As the amendments to the claims are fully supported by the application as filed, no new matter is presented by the amendments.

The present paper further presents new claim 67. Claim 67 is fully supported by the application as filed and therefore presents no new matter. Specifc support for new claim 67 may be found, for example, in the specification at page 35, lines 3-5, page 37, lines 21-22, page 40, lines 6-13, page 48, lines 1-5 and lines 8-11, and at page 127, lines 1-20 and Table 7. Accordingly, claim 67 is fully supported by the application as filed and presents no new matter.

Entry of the amendments to the claims is therefore respectfully requested under 37 C.F.R. § 1.111.

II. The Objection to the Specification

The specification stands objected to because of an alleged inconsistency between Genbank Accession No. NM_005577.1 and the nucleic acid sequence provided as SEQ ID NO.:4. In particular, the PTO contends that Genbank Accession No. NM_005577.1 describes a nucleotide sequence only 6489 nucleotides in length, substantially shorter than SEQ ID NO.:4.

In response, Applicants respectfully invite the PTO's attention to Exhibit 1, providing the nucleotide sequence identified as Genbank Accession No. NM_005577.1. Applicants note that Genbank has updated this accession number with a second sequence, Genbank Accession No. NM_005577.**2** and believe that the PTO may have inadvertently viewed the replacement sequence rather than the original. In any event, Applicants believe that Genbank Accession No. NM_005577.1 and SEQ ID NO.:4 define the same sequence and that there is no discrepancy. Accordingly, Applicants respectfully request that the objection to the specification be withdrawn.

III. The Objections to the Claims

Claim 50 stands objected to for reciting SEQ ID NO.: 95 twice. Claim 50 has been amended to correct this error. Thus, Applicants believe this objection is moot and respectfully request its withdrawal.

Claims 52 and 53 stand objected to as depending from a rejected independent claim, but otherwise allowable. Applicants believe these objections are moot in view of the amendments to the claims and request their withdrawal.

III. The Rejection of Claim 50 Under 35 U.S.C. § 112, Second Paragraph

Claim 50 stands rejected under 35 U.S.C. § 112, second paragraph, as indefinite as the claimed compound allegedly cannot comprise a sequence selected from a closed group of sequences. Without acquiescing to the propriety of the rejection, claim 50, as amended, no longer recites compounds that comprise a sequence selected from a closed group of sequences. As such, Applicants believe the rejection is moot and respectfully request its withdrawal.

IV. The Rejection of Claims 1, 3, and 17 Under 35 U.S.C. § 102(e)

Claims 1, 3, and 17 stand rejected as allegedly anticipated under 35 U.S.C. § 102(e) by Cai *et al.* (International Patent Publication No. WO 2004/108916). In particular, the PTO contends that Cai *et al.* teaches an antisense oligonucleotide of which nucleotides 2-26 are 96% complementary to nucleotides 12,805-12,829 of SEQ ID NO.:4 as recited by, for example, claim 1. Thus, according to the PTO, Cai *et al.* anticipates claims 1, 3, and 17.

In response, Applicants respectfully submit that Cai *et al.* cannot anticipate claim 1, and thus claims 3 and 17 depending therefrom, as currently amended. First, the oligonucleotide of Cai *et al.* is 26 nucleotides long, yet the PTO's calculation of percent complementarity between the oligonucleotide of Cai *et al.* and the present SEQ ID NO.:4 ignores the mismatch at position 1 of the oligonucleotide of Cai *et al.* Each nucleotide of the oligonucleotide of Cai *et al.* should be considered when calculating the percentage of complementarity. When each nucleotide of the oligonucleotide of Cai *et al.* is so considered, this oligonucleotide is calculated to be 92.3% complementary to SEQ ID NO.: 4.

Claim 1 recites an antisense compound that is at least 94% complementary to nucleotides 12380-13493 of SEQ ID NO.:4. As the oligonucleotide of Cai *et al.* is less than 94% identical to this sequence, it does not teach this element of claim 1. As such, Cai *et al.* cannot anticipate claim 1 as amended, or claims 3 and 17 depending therefrom, since it fails to teach each and every element of the invention as presently claimed. *See Merck & Co. v. Teva Pharmaceuticals USA, Inc.*, 68 USPQ2d 185 (Fed. Cir. 2003). Accordingly, Applicants assert that the rejection of claims 1, 3, and 17 as anticipated by Cai *et al.* is moot in view of the amendments to the claims and therefore request its withdrawal.

V. The Rejection of Claims 1, 3, and 17 Under 35 U.S.C. § 103(a)

Claims 1, 3, 6, 8-11, 17, 54-60, and 62-66 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over Ruoy *et al.* (International Patent Publication No. WO 99/65241) in view of Morishita *et al.* (*Circulation*, 1998, 98:1898-1904) and Baracchini *et al.* (U.S. Patent No. 5,801,154). Claims 1, 3, 6, 8-11, 17, and 54-66 further stand rejected in view of this combination of references in further view of Ramasamy *et al.* (U.S. Patent No. 6,525,191).

In particular, the PTO contends that Ruoy *et al.* teaches antisense nucleic acids targeted to apolipoprotein(a) and use of such antisense nucleic acids to downregulate gene expression. The PTO acknowledges that Ruoy does not teach antisense compounds that are at least 90% complementary to the coding region of apolipoprotein(a). However, the PTO contends that Morishita *et al.* teaches phosphorothioate modified ribozymes and a DNA oligonucleotide targeted to the coding region of kringle 4 of apolipoprotein(a). The PTO relies on Baracchini *et al.* and Ramasamy *et al.* to teach various chemical modifications of oligonucleotides (*e.g.*, phosphorothioates, 2'-O-methoxyethyl sugar moieties, bicyclic nucleic acid sugar moieties, *etc.*). The PTO further contends that Baracchini states that the coding region of a gene is a preferred target for antisense modulation. Thus, according to the PTO, it would be obvious to one of ordinary skill in the art to make an antisense oligonucleotide to apolipoprotein(a) in view of the combination of Ruoy *et al.*, Morishita *et al.*, and Baracchini *et al.*

In response, Applicants respectfully submit that none of the references, either alone or in combination, provides a reason for one of ordinary skill in the art to select the particular region of the coding sequence of apolipoprotein(a) presently recited by independent claims 1 and 57. Further, Morishita *et al.*, as discussed below, specifically teaches away from antisense modulation of apolipoprotein(a), further demonstrating the non-obviousness of the claims.

A. The Legal Standard

The Supreme Court's decision in *Graham* v. *John Deere Co. of Kansas City*, 383 U.S.1 (1966) sets forth the controlling standard for assessing purported obviousness of a claimed invention: "[T]he scope and content of the prior art are ... determined; differences between the prior art and the claims at issue are ... ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background the obviousness or nonobviousness of the subject matter is determined." *See id.* at 17–18.

The Supreme Court's recent decision in *KSR. Int'l Co. v.Teleflex*, 127 S.Ct. 1727, (2007) provides guidance regarding exactly how the differences between the prior art and claimed invention are analyzed to assess the obviousness or non-obviousness of the claims. As the Supreme Court explained, "interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art" can all be assessed "to determine whether there was an apparent reason to combine the known elements" as recited by the claim at issue. *See id.* at 1731 (2007) . The Supreme Court expressly cautioned that this reason should be explicitly stated. *See id.* Thus, the PTO must identify an explicit reason to combine the elements of the prior art in the manner defined by the claims at issue.

Moreover, the prior art must be considered in its entirety, including portions of the prior art that teach away from the claimed subject matter. *See W.L. Gore & Associates, Inc. v. Garlock Inc.*, 220 USPQ 303 (Fed. Cir. 1984). A reference may be said to teach away when a person of ordinary skill, upon reading the reference,... would be led in a direction divergent from that taken by the applicant." *See Tec Air, Inc. v. Denso Mfg. Mich. Inc.*, 52 USPQ2d 1294, 1298, (Fed. Cir. 1999), quoted by *In re Haruna*, 58 USPQ2d 1517 (Fed. Cir. 2001).

Prior art references that teach away from the claimed combination should not be combined. *See In re Grasselli*, 218 USPQ 769 (Fed. Cir. 1983). Thus, if a prior art reference "did in fact teach away from [another prior art reference], then that finding alone can defeat

[an] obviousness" attack based on the combination of the two references. *See Winner International Royalty Corp. v. Wang*, 53 USPQ2d 1580 (Fed. Cir. 2000).

Further, "known disadvantages... that would naturally discourage search for new inventions may be taken into account in determining obviousness." *See United States v. Adams*, 383 U.S. 39, 52; 148 USPQ 479, 484 (1966). In fact, the inventor's achievement of the claimed invention by doing what others suggested should not be done is a fact strongly probative of nonobviousness. *See Kloser Speedsteel AB v. Crucible Inc.*, 230 USPQ 81 (Fed. Cir. 1986), *on rehearing* 231 USPQ 160 (Fed. Cir. 1986).

B. The Cited References Do Not Suggest an Antisense Compound at Least 90% or 94% Complementary to Nucleotides 12380-13493 of SEQ ID NO: 4

None of the cited references, either alone or in combination, teach or suggest an antisense compound at least 90% or 94% complementary to nucleotides 12380-13493 of SEQ ID NO: 4. Ruoy *et al.* neither teaches nor suggests that an antisense compound should be targeted to any particular region of the coding region of apolipoprotein(a). Further, as discussed extensively below, Morishita *et al.* teaches that antisense compounds, whether targeted to the coding region or otherwise, should not be used to modulate apolipoprotein(a) expression. As such, the combination of Ruoy *et al.* and Morishita *et al.* certainly fails to provide a reason why one of ordinary skill in the art should select the particular 1113 nucleotide region out of more than 13,000 nucleotides of SEQ ID NO.: 4 as a target for antisense modulation.

Moreover, neither Baracchini *et al.* nor Ramasamy *et al.* disclose anything regarding antisense modulation of apolipoprotein(a) expression. Rather, these references merely teach various chemical modifications of oligonucleotides and, in the case of Baracchini *et al.*, provides general teaching that antisense compounds can be targeted to the coding region of a gene. As such, neither of these references cure the deficiencies of Ruoy *et al.* and Morishita *et al.* discussed above. Accordingly, the combination of references, when considered as a whole, fails to teach or suggest each and every element of the invention as presently claimed. Further, the PTO has failed to identify a reason as required by the Supreme Court in *KSR v. Teleflex* "that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does." *See KSR* at 1731. Therefore, Applicants respectfully submit that the PTO has failed to establish *prima facie* obviousness of the claimed invention.

C. Morishita *et al.* Teaches Away from the Claimed Invention

In addition, Morishita *et al.* specifically teaches away from antisense modulation of apolipoprotein(a) expression. At the paragraph bridging pages 1898 and 1899 of Morishita *et*

al., the authors consider whether to use antisense compounds or ribozymes to modulate apolipoprotein(a) expression. Morishita *et al.* concludes that ribozymes are superior to antisense compounds for modulating expression of this gene because, according to Morishita *et al.*, ribozymes are more effective for inhibiting target gene expression and because of the difficulty of using antisense compounds to selectively inhibit apolipoprotein(a) expression.

Indeed, Morishita *et al.* uses a DNA oligonucleotide without ribozyme activity as a negative control (*see* Morishita *et al.* at page 1899, under the heading "Synthesis of Ribozyme ON and Selection of Sequence Targets." This DNA oligonucleotide did not in fact inhibit apolipoprotien(a) expression. *See* Morishita *et al.* at page 1901, Figure 2. Therefore, Morishita *et al.* teaches that ribozymes, rather than antisense compounds as recited by the present claims, should be used to modulate apolipoprotein(a) expression and thus teaches away from the invention as presently claimed.

Since Morishita *et al.* teaches away from antisense compounds targeted to apolipoprotein(a), it is improper to include Morishita *et al.* in an obviousness rejection of claims drawn to such antisense compounds. *See In re Grasselli* and *Winner International.* Further, the conclusion of Morishita *et al.* that antisense compounds targeted to apolipoprotein(a) should not be used to modulate apolipoprotein(a) expression is strongly probative of the nonobviousness of Applicants' invention. *See Kloser Speedsteel.* Accordingly, Applicants respectfully submit that Morishita *et al.* actually provides evidence that the claimed antisense compounds are not obvious, contrary to the PTO's assertion otherwise.

D. The Obviousness Rejections Should Be Withdrawn

Applicants respectfully submit that the references cited by the PTO, whether considered alone or in combination, fail to teach or suggest each and every element of the invention recited by the independent claims, claims 1 and 57, of the present application. As such, Applicants respectfully submit that claims 1 and 57, and each of the claims depending therefrom, are not obvious over the references cited by the PTO. Therefore, Applicants respectfully request that the rejection of claims 1, 3, 6, 8-11, 17, 54-60, and 62-66 under 35 U.S.C. § 103(a) as obvious over Ruoy *et al.* in view of Morishita *et al.* and Baracchini *et al.* and of claims 1, 3, 6, 8-11, 17, and 54-66 over this combination of references in further view of Ramasamy *et al.* be withdrawn.

VI. Double Patenting

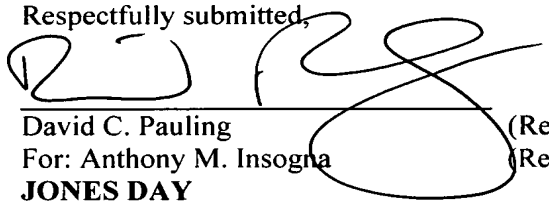
Claims 1, 3, 6, 8-11, and 54-57 stand provisionally rejected under the doctrine of obviousness-type double patenting over claims 1, 2, and 4-11 of copending application no. 10/485,113. Without acquiescing to the propriety of the rejection, Applicants believe the

rejection is moot in view of the abandonment of copending application no. 10/485,113. Accordingly, Applicants respectfully request that the provisional rejection of claims 1, 3, 6, 8-11, and 54-57 for obviousness-type double patenting be withdrawn.

VII. Conclusion

In light of the above amendments and remarks, Applicants respectfully request that the PTO reconsider this application with a view towards allowance. The Examiner is invited to call the undersigned attorney at(650) 739-3949, if a telephone call could help resolve any remaining items.

Respectfully submitted,



Date: August 14, 2007

56,056

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EXHIBIT 1

Genbank Accesion No. NM_005577.1

1: NM_005577. Reports ...[gi:5031884] The record has been replaced by 116292749

Comment Features Sequence

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LOCUS       NM_005577              13938 bp    mRNA    linear   PRI 19-SEP-2006
DEFINITION  Homo sapiens lipoprotein, Lp(a) (LPA), mRNA.
ACCESSION   NM_005577 XM_926329 XM_941794
VERSION     NM_005577.1  GI:5031884
KEYWORDS    .
SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Euarchontoglires; Primates; Haplorrhini;
            Catarrhini; Hominidae; Homo.
REFERENCE   1  (bases 1 to 13938)
  AUTHORS   Becker,L., Nesheim,M.E. and Koschinsky,M.L.
  TITLE     Catalysis of covalent Lp(a) assembly: evidence for an extracellular
            enzyme activity that enhances disulfide bond formation
  JOURNAL   Biochemistry 45 (32), 9919-9928 (2006)
   PUBMED   16893192
  REMARK    GeneRIF: Cultured human hepatoma cells secrete an oxidase activity
            that dramatically enhances the rate of covalent Lp(a) assembly.
REFERENCE   2  (bases 1 to 13938)
  AUTHORS   Sotiriou,S.N., Orlova,V.V., Al-Fakhri,N., Ihanus,E.,
            Economopoulou,M., Isermann,B., Bdeir,K., Nawroth,P.P.,
            Preissner,K.T., Gahmberg,C.G., Koschinsky,M.L. and Chavakis,T.
  TITLE     Lipoprotein(a) in atherosclerotic plaques recruits inflammatory
            cells through interaction with Mac-1 integrin
  JOURNAL   FASEB J. 20 (3), 559-561 (2006)
   PUBMED   16403785
  REMARK    GeneRIF: data demonstrate that Lp(a), via its apo(a) moiety, is a
            ligand for the beta2-integrin Mac-1, thereby facilitating
            inflammatory cell recruitment to atherosclerotic plaques; these
            observations suggest a novel mechanism for atherogenic properties
            of Lp(a)
REFERENCE   3  (bases 1 to 13938)
  AUTHORS   Unluhizarci,K., Muhtaroglu,S., Kabak,S., Bayram,F. and
            Kelestimur,F.
  TITLE     Serum lipoprotein (a) levels in patients with diabetic foot lesions
  JOURNAL   Diabetes Res. Clin. Pract. 71 (2), 119-123 (2006)
   PUBMED   16122830
  REMARK    GeneRIF: Lp (a) levels may have a pathogenetic role in the
            development of gangrenous foot lesions in patients with diabetes
            mellitus.
REFERENCE   4  (bases 1 to 13938)
  AUTHORS   Edelstein,C., Yousef,M. and Scanu,A.M.
  TITLE     Elements in the C terminus of apolipoprotein [a] responsible for
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the binding to the tenth type III module of human fibronectin
JOURNAL J. Lipid Res. 46 (12), 2673-2680 (2005)
PUBMED 16150826
REMARK GeneRIF: binding sites responsible for binding to fibronection
REFERENCE 5 (bases 1 to 13938)
AUTHORS Devlin,C.M., Lee,S.J., Kuriakose,G., Spencer,C., Becker,L., Grosskopf,I., Ko,C., Huang,L.S., Koschinsky,M.L., Cooper,A.D. and Tabas,I.
TITLE An apolipoprotein(a) peptide delays chylomicron remnant clearance and increases plasma remnant lipoproteins and atherosclerosis in vivo
JOURNAL Arterioscler. Thromb. Vasc. Biol. 25 (8), 1704-1710 (2005)
PUBMED 15905467
REMARK GeneRIF: high levels of apo(a)/Lp(a), perhaps acting via a specific cell-surface binding domain, inhibit hepatic clearance of remnants, leading to high plasma levels of remnant lipoproteins and markedly enhanced atherosclerosis
REFERENCE 6 (bases 1 to 13938)
AUTHORS Nardulli,M., Durlach,V., Pepe,G. and Angles-Cano,E.
TITLE Mechanism for the homocysteine-enhanced antifibrinolytic potential of lipoprotein(a) in human plasma
JOURNAL Thromb. Haemost. 94 (1), 75-81 (2005)
PUBMED 16113787
REMARK GeneRIF: lipoprotein(a) has a role in homocysteine-enhanced antifibrinolysis in human plasma
REFERENCE 7 (bases 1 to 13938)
AUTHORS Song,K.H., Ko,S.H., Kim,H.W., Ahn,Y.B., Lee,J.M., Son,H.S., Yoon,K.H., Cha,B.Y., Lee,K.W. and Son,H.Y.
TITLE Prospective study of lipoprotein(a) as a risk factor for deteriorating renal function in type 2 diabetic patients with overt proteinuria
JOURNAL Diabetes Care 28 (7), 1718-1723 (2005)
PUBMED 15983325
REMARK GeneRIF: Lp(a) is an independent risk factor for the progression of diabetic nephropathy in type 2 diabetic patients with overt proteinuria.
REFERENCE 8 (bases 1 to 13938)
AUTHORS Schneider,M., Witztum,J.L., Young,S.G., Ludwig,E.H., Miller,E.R., Tsimikas,S., Curtiss,L.K., Marcovina,S.M., Taylor,J.M., Lawn,R.M., Innerarity,T.L. and Pitas,R.E.
TITLE High-level lipoprotein [a] expression in transgenic mice: evidence for oxidized phospholipids in lipoprotein [a] but not in low density lipoproteins
JOURNAL J. Lipid Res. 46 (4), 769-778 (2005)
PUBMED 15654123
REMARK GeneRIF: mechanism by which increased circulating levels of Lp[a] could contribute to atherogenesis
REFERENCE 9 (bases 1 to 13938)
AUTHORS Eliassen,K.A., Brodal,B.P., Svindland,A., Osmundsen,H., Ronning,H., Djurovic,S. and Berg,K.
TITLE Activity of peroxisomal enzymes, and levels of polyamines in LPA-transgenic mice on two different diets
JOURNAL (er) Lipids Health Dis 4, 23 (2005)
PUBMED 16202171
REMARK GeneRIF: Suggest connection between peroxisomal enzyme activity & presence of human LPA gene in murine genome. Effect may be result of changes in oxidative processes in lipid metabolism rather than from direct effect of LPA gene on peroximal gene expression.
REFERENCE 10 (bases 1 to 13938)
AUTHORS Parson,W., Kraft,H.G., Niederstatter,H., Lingenhel,A.W., Kochl,S.,

Fresser,F. and Utermann,G.
TITLE A common nonsense mutation in the repetitive Kringle IV-2 domain of human apolipoprotein(a) results in a truncated protein and low plasma Lp(a)
JOURNAL Hum. Mutat. 24 (6), 474-480 (2004)
PUBMED 15523644
REFERENCE 11 (bases 1 to 13938)
AUTHORS Lamanuzzi,L.B., Mtairag el,M., Pepe,G. and Angles-Cano,E.
TITLE Neutrophils stimulated by apolipoprotein(a) generate fragments that are stronger inhibitors of plasmin formation than apo(a)
JOURNAL Thromb. Haemost. 92 (5), 1066-1075 (2004)
PUBMED 15543335
REMARK GeneRIF: Stimulation of PMNs by apo(a) results in the formation of elastase-derived apo(a) fragments that produce a concentration-dependent decrease in the formation of plasmin
REFERENCE 12 (bases 1 to 13938)
AUTHORS Diaz-Peromingo,J.A., Carbajal,D.G. and Alban-Salgado,A.
TITLE Lipoprotein (a) in patients on hemodialysis
JOURNAL Acta Med. Austriaca 31 (3), 73-75 (2004)
PUBMED 15515480
REMARK GeneRIF: Changes in Lp(a) levels were found and perhaps these changes may be related to the episodic inflammation affecting patients on hemodialysis.
REFERENCE 13 (bases 1 to 13938)
AUTHORS Anderson,N.L., Polanski,M., Pieper,R., Gatlin,T., Tirumalai,R.S., Conrads,T.P., Veenstra,T.D., Adkins,J.N., Pounds,J.G., Fagan,R. and Lobley,A.
TITLE The human plasma proteome: a nonredundant list developed by combination of four separate sources
JOURNAL Mol. Cell Proteomics 3 (4), 311-326 (2004)
PUBMED 14718574
REFERENCE 14 (bases 1 to 13938)
AUTHORS Frohlich,J., Dobiasova,M., Adler,L. and Francis,M.
TITLE Gender differences in plasma levels of lipoprotein (a) in patients with angiographically proven coronary artery disease
JOURNAL Physiol Res 53 (5), 481-486 (2004)
PUBMED 15479125
REMARK GeneRIF: Our findings suggest that Lp(a) is more strongly associated with aCAD+ in women than in men.
REFERENCE 15 (bases 1 to 13938)
AUTHORS Bogavac-Stanojevic,N., Djurovic,S., Jelic-Ivanovic,Z., Spasojevic-Kalimanovska,V. and Kalimanovska-Ostric,D.
TITLE Circulating transforming growth factor-beta1, lipoprotein(a) and cellular adhesion molecules in angiographically assessed coronary artery disease
JOURNAL Clin. Chem. Lab. Med. 41 (7), 893-898 (2003)
PUBMED 12940514
REMARK GeneRIF: Blood levels are higher in coronary artery disease patients compared with normal values.
REFERENCE 16 (bases 1 to 13938)
AUTHORS Gazzaruso,C., Garzaniti,A., Falcone,C., Puija,A., Geroldi,D., Giordanetti,S. and Fratino,P.
TITLE Lipoprotein(a), apolipoprotein(a) polymorphism and restenosis after intracoronary stent placement in Type 2 diabetic patients
JOURNAL J. Diabetes Complicat. 17 (3), 135-140 (2003)
PUBMED 12738397
REMARK GeneRIF: Lp(a) and apo(a) polymorphisms do not appear to be reliable markers of restenosis in patients with Type 2 diabetes mellitus.
REFERENCE 17 (bases 1 to 13938)

AUTHORS Nassir,F., Xie,Y. and Davidson,N.O.
TITLE Apolipoprotein[a] secretion from hepatoma cells is regulated in a size-dependent manner by alterations in disulfide bond formation
JOURNAL J. Lipid Res. 44 (4), 816-827 (2003)
PUBMED 12562843

REFERENCE 18 (bases 1 to 13938)
AUTHORS Tian,H., Han,L., Ren,Y., Li,X. and Liang,J.
TITLE Lipoprotein(a) level and lipids in type 2 diabetic patients and their normoglycemic first-degree relatives in type 2 diabetic pedigrees
JOURNAL Diabetes Res. Clin. Pract. 59 (1), 63-69 (2003)
PUBMED 12482643
REMARK GeneRIF: Positive correlation of Lp(a) between type 2 diabetic patients and their offspring, suggesting a potential genetic control for Lp(a) levels in type 2 diabetics families.

REFERENCE 19 (bases 1 to 13938)
AUTHORS Barre,D.E.
TITLE Apolipoprotein (a) mediates the lipoprotein (a)-induced biphasic shift in human platelet cyclic AMP
JOURNAL Thromb. Res. 112 (5-6), 321-324 (2003)
PUBMED 15041277
REMARK GeneRIF: apo(a) mediates the Lp(a)-induced biphasic response in platelet c-AMP as the result of platelet exposure to increasing levels of Lp(a), up to a concentration of 25 mg/dl Lp(a)

REFERENCE 20 (bases 1 to 13938)
AUTHORS Kapetanopoulos,A., Fresser,F., Millonig,G., Shaul,Y., Baier,G. and Utermann,G.
TITLE Direct interaction of the extracellular matrix protein DANCE with apolipoprotein(a) mediated by the kringle IV-type 2 domain
JOURNAL Mol. Genet. Genomics 267 (4), 440-446 (2002)
PUBMED 12111551

REFERENCE 21 (bases 1 to 13938)
AUTHORS Nawawi,H.M., Muhajir,M., Kian,Y.C., Mohamud,W.N., Yusoff,K. and Khalid,B.A.
TITLE Type of diabetes and waist-hip ratio are important determinants of serum lipoprotein (a) levels in diabetic patients
JOURNAL Diabetes Res. Clin. Pract. 56 (3), 221-227 (2002)
PUBMED 11947970
REMARK GeneRIF: Type of diabetes and waist-hip ratio are important determinants of levels in diabetic patients [LIPOPROTEIN (A)]

REFERENCE 22 (bases 1 to 13938)
AUTHORS Cerrato,P., Imperiale,D., Fornengo,P., Bruno,G., Cassader,M., Maffeis,P., Cavallo Perin,P., Pagano,G. and Bergamasco,B.
TITLE Higher lipoprotein (a) levels in atherothrombotic than lacunar ischemic cerebrovascular disease
JOURNAL Neurology 58 (4), 653-655 (2002)
PUBMED 11865151
REMARK GeneRIF: Lipoprotein (a) promotes large vessel atheromatosis rather than small vessel arteriolosclerosis and favors thrombosis on atheromatous plaques by suppressing local fibrinolysis.

REFERENCE 23 (bases 1 to 13938)
AUTHORS Geethanjali,F.S., Jose,V.J. and Kanagasabapathy,A.S.
TITLE Lipoprotein (a) phenotypes in south Indian patients with coronary artery disease
JOURNAL Indian Heart J 54 (1), 50-53 (2002)
PUBMED 11999088
REMARK GeneRIF: Plasma lipoprotein (a) levels are significantly elevated in patients with coronary artery disease as compared to controls. The contribution of lipoprotein (a) phenotype to the lipoprotein (a) levels in our population, if any, is modest.

REFERENCE 24 (bases 1 to 13938)
AUTHORS Cabrinety,N., Pisonero,M.J., Ajram,J., Armenteras,A. and Cuatrecasas,J.M.
TITLE Lipoprotein (a) in obese children with a family history of cardiovascular disease
JOURNAL J. Pediatr. Endocrinol. Metab. 15 (1), 77-80 (2002)
PUBMED 11822583
REMARK GeneRIF: children's group with BMI > 30 and with family history of CVD presented higher levels in comparison to the less obese group with family history of CVD
REFERENCE 25 (bases 1 to 13938)
AUTHORS Xue,S., Madison,E.L. and Miles,L.A.
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PUBMED 11816712
REMARK GeneRIF: The Apo(a) Kringle V-protease domain binds to plasmin-treated fibrinogen, competing with and sharing binding sites with Lp(a), and possibly participating in the Lp(a)-fibrinogen interaction.
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AUTHORS Ogorelkova,M., Kraft,H.G., Ehnholm,C. and Utermann,G.
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AUTHORS Klose,R., Fresser,F., Kochl,S., Parson,W., Kapetanopoulos,A., Fruchart-Najib,J., Baier,G. and Utermann,G.
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AUTHORS Rosby,O. and Berg,K.
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REFERENCE 29 (bases 1 to 13938)
AUTHORS Ogorelkova,M., Gruber,A. and Utermann,G.
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AUTHORS Edelstein,C., Shapiro,S.D., Klezovitch,O. and Scanu,A.M.
TITLE Macrophage metalloelastase, MMP-12, cleaves human apolipoprotein(a) in the linker region between kringles IV-4 and IV-5. Potential relevance to lipoprotein(a) biology
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REFERENCE 31 (bases 1 to 13938)
AUTHORS Niemeier,A., Willnow,T., Dieplinger,H., Jacobsen,C., Meyer,N., Hilpert,J. and Beisiegel,U.
TITLE Identification of megalin/gp330 as a receptor for lipoprotein(a) in vitro
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REFERENCE 32 (bases 1 to 13938)
AUTHORS Bonen,D.K., Nassir,F., Hausman,A.M. and Davidson,N.O.
TITLE Inhibition of N-linked glycosylation results in retention of intracellular apo[a] in hepatoma cells, although nonglycosylated and immature forms of apolipoprotein[a] are competent to associate with apolipoprotein B-100 in vitro
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AUTHORS Kochl,S., Fresser,F., Lobentanz,E., Baier,G. and Utermann,G.
TITLE Novel interaction of apolipoprotein(a) with beta-2 glycoprotein I mediated by the kringle IV domain
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AUTHORS Edelstein,C., Italia,J.A. and Scanu,A.M.
TITLE Polymorphonuclear cells isolated from human peripheral blood cleave lipoprotein(a) and apolipoprotein(a) at multiple interkringle sites via the enzyme elastase. Generation of mini-Lp(a) particles and apo(a) fragments
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AUTHORS Edelstein,C., Italia,J.A., Klezovitch,O. and Scanu,A.M.
TITLE Functional and metabolic differences between elastase-generated fragments of human lipoprotein[a] and apolipoprotein[a]
JOURNAL J. Lipid Res. 37 (8), 1786-1801 (1996)
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AUTHORS Grainger,D.J., Kemp,P.R., Liu,A.C., Lawn,R.M. and Metcalfe,J.C.
TITLE Activation of transforming growth factor-beta is inhibited in transgenic apolipoprotein(a) mice
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REFERENCE 37 (bases 1 to 13938)
AUTHORS Salonen,E.M., Jauhiainen,M., Zardi,L., Vaheri,A. and Ehnholm,C.
TITLE Lipoprotein(a) binds to fibronectin and has serine proteinase activity capable of cleaving it
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PUBMED 2531657
REFERENCE 38 (bases 1 to 13938)
AUTHORS Frank,S.L., Klisak,I., Sparkes,R.S., Mohandas,T., Tomlinson,J.E., McLean,J.W., Lawn,R.M. and Lusis,A.J.
TITLE The apolipoprotein(a) gene resides on human chromosome 6q26-27, in close proximity to the homologous gene for plasminogen
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REFERENCE 39 (bases 1 to 13938)
AUTHORS McLean,J.W., Tomlinson,J.E., Kuang,W.J., Eaton,D.L., Chen,E.Y., Fless,G.M., Scanu,A.M. and Lawn,R.M.
TITLE cDNA sequence of human apolipoprotein(a) is homologous to plasminogen
JOURNAL Nature 330 (6144), 132-137 (1987)
PUBMED 3670400
COMMENT PROVISIONAL REFSEQ: This record has not yet been subject to final NCBI review. The reference sequence was derived from X06290.1.
[WARNING] On Oct 20, 2006 this sequence was replaced by gi:116292749.
On or before Mar 4, 2006 this sequence version replaced

gi:88998565, gi:88999541.

FEATURES Location/Qualifiers

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